4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-N-0515]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Postmarketing Adverse Experience Reporting and Recordkeeping for Drug and Biological Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Submit written comments (including recommendations) on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be submitted to https://www.reginfo.gov/public/do/PRAMain. Find this particular information collection by selecting "Currently under Review - Open for Public Comments" or by using the search function. The OMB control number for this information collection is 0910-0230. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Postmarketing Adverse Experience Reporting and Recordkeeping for Drug and Biologics Products

OMB Control Number 0910-0230--Revision

This information collection supports statutory provisions set forth in the Federal Food, Drug, and Cosmetic Act (FD&C Act) regarding the monitoring of FDA-regulated products. Specifically, FDA must be promptly informed of adverse experiences associated with the use of marketed drugs, including human drugs and biological products. Regulations in §§ 310.305 and 314.80 (21 CFR 310.305 and 314.80) implement reporting and recordkeeping requirements that enable FDA to take action to protect the public health from adverse drug experiences. All applicants who have received marketing approval for drug products are required to report serious, unexpected adverse drug experiences (15-day "Alert reports"), as well as followup reports (§ 314.80(c)(1)) to FDA. This includes reports of all foreign or domestic adverse experiences as well as those based on information from applicable scientific literature and certain reports from postmarketing studies. Section 314.80(c)(1)(iii) pertains to such reports submitted by nonapplicants.

Under § 314.80(c)(2), applicants must provide periodic reports of adverse drug experiences. For the reporting interval, a periodic report includes reports of serious, expected adverse drug experiences, all nonserious adverse drug experiences, and an index of these reports; a narrative summary and analysis of adverse drug experiences; an analysis of the 15-day Alert reports submitted during the reporting interval; and a history of actions taken because of adverse drug experiences. Under § 314.80(j), applicants must keep for 10 years records of all adverse drug experience reports known to the applicant.

For marketed prescription drug products without approved new drug applications (NDAs) or abbreviated new drug applications (ANDAs), manufacturers, packers, and distributors are

required to report to FDA serious, unexpected adverse drug experiences as well as followup reports (§ 310.305(c)). Section 310.305(c)(5) pertains to the submission of followup reports to reports forwarded to the manufacturers, packers, and distributors by FDA. Under § 310.305(g), each manufacturer, packer, and distributor shall maintain for 10 years records of all adverse drug experiences required to be reported.

Section 760 of the FD&C Act (21 U.S.C. 379aa) also provides for mandatory safety reporting for over-the-counter (OTC) human drug products not subject to applications approved under section 505 of the FD&C Act (21 U.S.C. 355) (NDAs or ANDAs). These requirements apply to all OTC drug products marketed without an approved application, including those marketed under the OTC Drug Monograph Review process (whether or not subject to a final monograph), those marketed outside the monograph system, and including those that have been discontinued from marketing but for which a report of an adverse event was received. Under 21 CFR 329.100, respondents must submit reports according to section 760 of the FD&C Act in an electronic format.

To assist respondents with implementation of section 760 of the FD&C Act, FDA developed the guidance for industry entitled "Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed Without an Approved Application," available at https://www.fda.gov/media/77193/download. The guidance document discusses what should be included in a serious adverse drug event report submitted under section 760(b)(1) of the FD&C Act, including how to submit these reports and followup reports under section 760(c)(2) of the FD&C Act.

Section 760(e) of the FD&C Act also requires that responsible persons maintain records of nonprescription drug adverse event reports, whether the event is serious or not, for a period of 6 years. FDA's guidance recommends that respondents maintain records of efforts to obtain the minimum data elements for a report of a serious adverse drug event and any followup reports.

The primary purpose of FDA's adverse drug experience reporting system is to enable identification of signals for potentially serious safety problems with marketed drugs. Although premarket testing discloses a general safety profile of a new drug's comparatively common adverse effects, the larger and more diverse patient populations exposed to the marketed drug provide the opportunity to collect information on rare, latent, and long-term effects. Signals are obtained from a variety of sources, including reports from patients, treating physicians, foreign regulatory agencies, and clinical investigators. Information derived from the adverse drug experience reporting system contributes directly to increased public health protection because the information enables FDA to make important changes to the product's labeling (such as adding a new warning), to make decisions about risk evaluation and mitigation strategies or the need for postmarketing studies or clinical trials and, when necessary, to initiate removal of a product from the market.

In addition, this information collection includes an International Council for Harmonisation (ICH) guidance for industry entitled "Providing Postmarketing Periodic Safety Reports in the ICH E2C(R2) Format (Periodic Benefit-Risk Evaluation Report)," available at https://www.fda.gov/media/85520/download. The guidance describes the conditions under which applicants may use the ICH3 E2C(R2) Periodic Benefit-Risk Evaluation Report format for certain types of adverse event reporting. FDA regulations in §§ 314.80(c)(2) and 600.80(c)(2) (21 CFR 600.80(c)(2)) require applicants to submit postmarketing periodic safety reports for each approved application. The reports must be submitted quarterly for the first 3 years following the U.S. approval date and annually thereafter and must contain the information described in §§ 314.80(c)(2)(ii) and 600.80(c)(2)(ii) (the information collection associated with 21 CFR part 600--Biological Products, is approved under OMB control number 0910-0308). The Agency guidance assists respondents with satisfying the regulatory requirements in an alternative format, noting that the process differs depending on whether an applicable periodic safety update report (PSUR) waiver is in place. The information collection

burden for waivers of a PSUR are currently approved in OMB control number 0910-0771; however, it is being consolidated with this information collection for administrative efficiency.

Similarly, the information collection accounts for burden that may be applicable to the guidance document, "Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During a Pandemic," available at https://www.fda.gov/media/72498/download. In response to the Coronavirus Disease 2019 public health emergency, we revised the Agency guidance document to provide recommendations for recordkeeping applicable to any pandemic, not just influenza, including recommendations for planning, notification, and documentation for continuity of operations for firms that report postmarketing adverse events during any pandemic.

Respondents to this collection of information are: (1) manufacturers, packers, distributors, and applicants of FDA-regulated drug and biologic products; (2) manufacturers, packers, and distributors of marketed prescription drug products without an FDA-approved application; and (3) manufacturers, packers, and distributors of marketed nonprescription drug products, including OTC drug products marketed without an approved application, OTC drug products marketed under the OTC Drug Monograph Review process (whether subject to a final monograph or not), and drug products marketed outside the monograph system.

In the *Federal Register* of June 30, 2021 (86 FR 34759), we published a 60-day notice requesting public comment on the proposed collection of information. No comments were received.

We estimate the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden[1]

21 CFR Section or Type of Respondent and Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
310.305(c)(5)	3	1	3	1	3
314.80(c)(1)(iii)	5	1	5	1	5
314.80(c)(2)	820	17.32	14,202	60	852,120
Reports of serious adverse drug events (§ 329.100)	285	690	196,650	6	1,179,900

Applicants that have a PSUR waiver for an approved application	55	3.4	187	1	187
Applicants that do not have a PSUR waiver for an approved application	29	2.3	67	2	134
Notifying FDA when normal reporting is not feasible	350	1	350	8	2,800
Total[2]			211,464		2,035,149

[1] The capital costs or operating and maintenance costs associated with this collection of information are approximately $25,000 annually.

Table 2.--Estimated Annual Recordkeeping Burden[1]

21 CFR Section or FD&C Act Section and Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
310.305	25	1	25	16	400
314.80(j)	352	1870	658,240	16	10,531,840
Recordkeeping of nonprescription drug adverse event reports (Section 760(e)(1) of the FD&C Act)	300	885.6667	265,700	8	2,125,600
Adding Adverse Event report planning to Continuity of Operations Plans	100	1	100	50	5,000
Maintaining documentation of pandemic conditions and resultant high absenteeism	350	1	350	8	2,800
Maintaining records to identify what reports have been stored and when the reporting process was restored.	350	1	350	8	2,800
Total[2]			924,765		12,668,440

[1] There are no capital costs or operating costs associated with this collection of information.

[2] There are maintenance costs of approximately $22,000 annually.

We have increased our estimate to reflect expected adjustments to the information collection since our last submission for OMB review and approval.

Dated: November 1, 2021.

Lauren K. Roth,

Associate Commissioner for Policy.

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